

We Claim:

1. An endosomolytic polymer comprising: a reversibly inhibited membrane active polymer.
2. The endosomolytic polymer of claim 1 wherein said reversibly inhibited membrane active polymer consists of a plurality of membrane activity inhibitors reversibly linked to a membrane active polyamine via pH labile bonds.
3. The endosomolytic polymer of claim 2 wherein said inhibitors consist of maleamates.
4. The endosomolytic polymer of claim 3 wherein said maleamates are derived from reaction of said membrane active polymer with maleic anhydrides selected from the group consisting of: CDM, CDM-thioester, and CDM-PEG.
5. The endosomolytic polymer of claim 2 wherein said inhibitors are cleaved from said polyamine in an endosome.
6. The endosomolytic polymer of claim 1 wherein said membrane active polymer has a molecular weight of at least about 10,000 Daltons.
7. A method for reversibly inhibiting membrane activity of a membrane active polyamine comprising: reacting said polyamine with a plurality of inhibitors wherein said inhibitors attach to said polyamine via cleavable pH-sensitive covalent bonds.
8. The method of claim 7 wherein said inhibitors are selected from the group consisting of: disubstituted maleic anhydride derivatives.
9. The method of claim 8 wherein said disubstituted maleic anhydride derivatives are selected from the groups consisting of: CDM, CDM-thioester and CDM-PEG.
10. The method of claim 7 wherein said polyamine has a molecular weight of at least about 10,000 daltons.
11. A composition for delivering a polynucleotide to a cell comprising: said polynucleotide associated with a reversibly inhibited membrane active polymer.
12. The composition of claim 11 wherein said composition consists of a nanoparticle.
13. The composition of claim 12 wherein said nanoparticle consists of a salt stable nanoparticle.
14. The composition of claim 11 wherein said reversibly inhibited membrane active polymer consists of a plurality of membrane activity inhibitors reversibly linked to a membrane active polyamine via pH labile bonds
15. The composition of claim 11 wherein said reversibly inhibited membrane active polymer is associated with said polynucleotide via electrostatic interaction.
16. The composition of claim 15 wherein said composition further comprises a polycation.

17. The composition of claim 16 wherein said reversibly inhibited membrane active polymer has a net negative charge
18. The composition of claim 17 wherein said polycation is crosslinked to said reversibly inhibited membrane active polyamine via a pH-labile bond.
19. A method for delivering a molecule to the cytoplasm of the cell comprising: associating said molecule with a reversibly inhibited membrane active polymer to form a complex and delivering said complex to said cell wherein said complex is endocytosed.
20. The method of claim 19 wherein said molecule consists of a polynucleotide.
21. The method of claim 20 further comprising: condensing said polynucleotide with a polycation to form a binary complex and recharging said binary complex by addition of said reversibly inhibited membrane active polymer to form a nanoparticle wherein said membrane active polymer is negatively charged.
22. The method of claim 21 wherein said polycation is crosslinked to said reversibly inhibited membrane active polymer via a pH-labile bond.
23. The method of claim 21 wherein said reversibly inhibited membrane active polymer disrupts an endocytic membrane thereby providing delivery of said molecule the cytoplasm of said cell.